

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application;

Listing of Claims:

1-5. (Canceled)

6. (Currently amended) A method to determine ~~clinical outcome of risk of cancer recurrence in a human subject having ER+ (estrogen receptor positive) breast cancer afflicted subject if treated with an antiestrogen agent against breast cancer~~, said method comprising
determining an expected cancer recurrence for said subject by assaying a sample of breast cancer cells from said subject for [[the]] a ratio of HoxB13 and IL17BR RNA expression levels that is higher than the mean (average) ratio of HoxB13 and IL17BR expression levels in ER+ breast cancer cells; or
determining an expected lack of cancer recurrence for said subject by assaying a sample of breast cancer cells from said subject for a ratio of HoxB13 and IL17BR RNA expression levels that is below the mean (average) ratio of HoxB13 and IL17BR RNA expression levels in ER+ breast cancer cells;
wherein said mean (average) ratio of HoxB13 and IL17BR RNA expression levels is determined from the mean (average) of HoxB13 RNA expression levels, and the mean (average) of IL17BR RNA expression levels, in ER+ breast cancer cell samples from human breast cancer subjects that respond to treatment with an antiestrogen agent against breast cancer and human breast cancer subjects that do not respond to treatment with said antiestrogen agent.

7. (Currently amended) The method of claim 6 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis or of survival outcome.

8. (Original) The method of claim 6 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).

9. (Currently amended) The method of claim 6 wherein said ~~sample of breast cancer cells is estrogen receptor positive (ER+)~~ assaying comprises determining the expression levels of HoxB13 and IL17BR mRNAs.

10. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids prepared by~~ mRNA amplification from said sample of breast cancer cells.

11. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids from said sample of breast cancer cells by~~ quantitative polymerase chain reaction (PCR).

12. (Currently amended) The method of ~~claim 6~~ claim 11 wherein said assaying ~~for the expression levels of HoxB13 and IL17BR~~ comprises ~~detection of HoxB13 and IL17BR proteins or proteolytic fragments of said proteins~~ real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a ΔC_t of the C_t values for HoxB13 and IL17BR RNA expression levels.

13. (Currently amended) The method of ~~claim 42~~ claim 6 wherein said sample is a formalin fixed paraffin embedded (FFPE) sample ~~detection of proteins or proteolytic fragments thereof~~ comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.

10. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids prepared by~~ mRNA amplification from said sample of breast cancer cells.

11. (Currently amended) The method of claim 6 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids from said sample of breast cancer cells by~~ quantitative polymerase chain reaction (PCR).

12. (Currently amended) The method of ~~claim 6~~ claim 11 wherein said assaying ~~for the expression levels of HoxB13 and IL17BR~~ comprises ~~detection of HoxB13 and IL17BR proteins or proteolytic fragments of said proteins~~ real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a ΔC_t of the C_t values for HoxB13 and IL17BR RNA expression levels.

13. (Currently amended) The method of ~~claim 42~~ claim 6 wherein said sample is a formalin fixed paraffin embedded (FFPE) sample ~~detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.~~

14. (Currently amended) A method of ~~determining prognosis to determine~~ outcome of a human subject having ER+ (estrogen receptor positive) breast cancer if treated with an antiestrogen agent against breast cancer, or of a human subject afflicted with breast cancer and treated with an antiestrogen agent against breast cancer, said method comprising:
assaying a sample of breast cancer cells from said subject, wherein
a for the ratio of HoxB13 and IL17BR RNA expression levels in a breast cancer cell
sample from said subject that is below the mean (average) ratio of HoxB13 and IL17BR expression levels
in ER+ breast cancer cells indicates a cancer-free outcome, and
a ratio above the mean (average) ratio of HoxB13 and IL17BR RNA expression levels in
ER+ breast cancer cells indicates an outcome comprising cancer recurrence;
wherein said mean (average) ratio of HoxB13 and IL17BR RNA expression levels is
determined from the mean (average) of HoxB13 RNA expression levels, and the mean (average) of
IL17BR RNA expression levels, in ER+ breast cancer cell samples from human breast cancer subjects
that respond to treatment with said antiestrogen agent against breast cancer and human breast cancer
subjects that do not respond to treatment with said antiestrogen agent.

15. (Currently amended) The method of claim 14 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis or of survival outcome.

16. (Original) The method of claim 14 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).

17. (Currently amended) The method of claim 14 wherein said ~~sample of breast cancer cells is ER+~~ assaying comprises determining the expression levels of HoxB13 and IL17BR mRNAs.

18. (Currently amended) The method of claim 14 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids prepared by mRNA~~ amplification from said sample of breast cancer cells.

19. (Currently amended) The method of claim 14 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids from said sample of breast cancer cells by~~ quantitative PCR.

20. (Currently amended) The method of ~~claim 14~~ claim 19 wherein said assaying ~~for the expression levels of HoxB13 and IL17BR~~ comprises ~~detection of HoxB13 and IL17BR proteins or proteolytic fragments of said proteins~~ real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a ΔC_t of the C_t values for HoxB13 and IL17BR RNA expression levels.

21. (Currently amended) The method of ~~claim 20~~ claim 14 wherein said sample is a formalin fixed paraffin embedded (FFPE) sample ~~detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.~~

22. (Original) The method of claim 14 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.

23. (Currently amended) A method to ~~determine therapeutic treatment for a breast cancer patient based upon said patient's~~ to predict an expected response or lack of response to treatment with an antiestrogen agent against breast cancer in a human ER+ (estrogen receptor positive) breast cancer patient, said method comprising

determining an expected response ~~or non-response~~ to treatment with an antiestrogen agent against breast cancer for said patient by assaying a sample of breast cancer cells from said patient for [[the]] a ratio of HoxB13 and IL17BR RNA expression levels that is higher than the mean (average) ratio of HoxB13 and IL17BR expression in ER+ breast cancer cells according to claim 6; and/or
determining an expected non-response to treatment with said antiestrogen agent against breast cancer for said patient by assaying a sample of breast cancer cells from said patient for a ratio of

HoxB13 and IL17BR RNA expression levels that is lower than the mean (average) ratio of HoxB13 and IL17BR expression in ER+ breast cancer cells and

selecting the appropriate treatment for a patient that is responsive or not responsive to treatment with said antiestrogen agent wherein said mean (average) ratio of HoxB13 and IL17BR RNA expression levels is determined from the mean (average) of HoxB13 RNA expression levels, and the mean (average) of IL17BR RNA expression levels, in ER+ breast cancer cell samples from human breast cancer subjects that respond to treatment with said antiestrogen agent against breast cancer and human breast cancer subjects that do not respond to treatment with said antiestrogen agent.

24. (Currently amended) The method of claim 23 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis or of survival outcome.

25. (Original) The method of claim 24 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).

26. (Currently amended) The method of claim 24 wherein said ~~sample of breast cancer cells is ER+~~ assaying comprises determining the expression levels of HoxB13 and IL17BR mRNAs.

27. (Currently amended) The method of claim 24 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids prepared by~~ mRNA amplification from said sample of breast cancer cells.

28. (Currently amended) The method of claim 24 wherein said assaying for the expression levels of HoxB13 and IL17BR RNA comprises ~~detection of nucleic acids from said sample of breast cancer cells by~~ quantitative PCR.

29. (Currently amended) The method of ~~claim 24~~ claim 28 wherein said assaying for the expression levels of HoxB13 and IL17BR comprises detection of HoxB13 and IL17BR proteins or proteolytic fragments of said proteins real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a ΔC_i of the C_i values for HoxB13 and IL17BR RNA expression levels.

30. (Currently amended) The method of ~~claim 29~~ claim 24 wherein said sample is a formalin fixed paraffin embedded (FFPE) sample ~~detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.~~

31. (Original) The method of claim 24 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.

32. (Currently amended) A method to determine ~~clinical outcome of risk of cancer recurrence in~~ a human subject having ER+ (estrogen receptor positive) breast cancer if treated with an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cells from said subject for

increased expression of HoxB13 sequences, or decreased expression of IL17BR sequences, relative to the mean (average) expression thereof in ER+ breast cancer cell samples from human breast cancer subjects that respond to treatment with said antiestrogen agent and human breast cancer subjects that do not respond to treatment with said antiestrogen agent, as an indicator of non-responsiveness to said agent; or

decreased expression of human HOXB13 sequences, or increased expression of IL17BR sequences, relative to the mean (average) expression thereof in ER+ breast cancer cell samples from human breast cancer subjects that respond to treatment with said antiestrogen agent and human breast cancer subjects that do not respond to treatment with said antiestrogen agent, as an indicator of responsiveness to said agent ~~or optionally another sequence the expression of which is correlated with their expression in breast cancer cells.~~

33. (Original) The method of claim 32 wherein said antiestrogen agent against breast cancer is selected from a selective estrogen receptor modulator (SERM), selective estrogen receptor downregulator (SERD), or aromatase inhibitor (AI).

34. (Previously presented) The method of claim 32 wherein said sample of breast cancer cells is ER+ or is obtained by a minimally invasive technique or selected from core biopsy,

excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.

35. (Currently amended) The method of claim 32 wherein said assaying for HoxB13 and/or IL17BR sequence expression comprises ~~detection of nucleic acids prepared by HoxB13 and/or IL17BR~~ mRNA amplification from said sample of breast cancer cells ~~or detection of nucleic acids from said sample of breast cancer cells by quantitative PCR.~~

36. (Currently amended) The method of claim 32 wherein said assaying ~~comprises quantitative PCR for expression~~ ~~comprises detection of proteins encoded by said sequences or proteolytic fragments of said proteins.~~

37. (Currently amended) The method of ~~claim 36~~ claim 32 wherein said ~~sample is a formalin fixed paraffin embedded (FFPE) sample~~ ~~detection of proteins or proteolytic fragments thereof comprises detection thereof in the blood of said subject or in breast cancer epithelial cells enriched from the blood of said subject.~~

38. (Currently amended) The method of claim 32 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 and/or IL17BR sequences.

39-41. (canceled)

42. (Currently amended) The method of ~~claim 32~~ claim 35 wherein said assaying comprises real-time PCR and said ratio of HoxB13 and IL17BR RNA expression levels is expressed as a ΔC_t of the C_t values for HoxB13 and IL17BR RNA expression levels ~~for expression~~ ~~comprises assaying for methylation of HoxB13 or IL17BR nucleic acid sequences.~~

43-48. (canceled)

49. (Currently amended) [[A]] The method of claim 6 wherein said assaying comprises detecting to determine clinical outcome of a human subject having breast cancer if treated with an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cells

~~from said subject for expression of an IL17BR sequence selected from SEQ ID NOs: 1, 2, 3, or 8, or 32-34.~~

50. (Currently amended) ~~[[A]] The method of claim 6 wherein said assaying comprises detecting to determine clinical outcome of a human subject having breast cancer if treated with an antiestrogen agent against breast cancer, said method comprising assaying a sample of breast cells from said subject for expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.~~

51. (canceled)

52. (Currently amended) ~~The method of claim 14 wherein said assaying is for comprises detecting~~ expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.

53. (Currently amended) ~~The method of claim 14 wherein said assaying is for comprises detecting~~ expression of an IL17BR sequence selected from SEQ ID NOS: 1, 2, 3, or 8, or 32-34.

54. (Currently amended) ~~The method of claim 23 wherein said assaying is for comprises detecting~~ expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.

55. (Currently amended) ~~The method of claim 23 wherein said assaying is for comprises detecting~~ expression of an IL17BR sequence selected from SEQ ID NOS: 1, 2, 3, or 8, or 32-34.

56. (Currently amended) ~~The method of claim 32 wherein said assaying is for comprises detecting~~ expression of a HoxB13 sequence selected from SEQ ID NOS: 6, 7, 10, 11-31, 35 or 37.

57. (Currently amended) ~~The method of claim 32 wherein said assaying is for comprises detecting~~ expression of an IL17BR sequence selected from SEQ ID NOS: 1, 2, 3, or 8, or 32-34.

58. (Previously presented) The method of claim 6 wherein said sample is obtained by a minimally invasive technique or selected from core biopsy, excisional biopsy, a ductal lavage sample, a fine needle aspiration sample, or cells microdissected from said sample.

59. (Previously presented) The method of claim 32 wherein said expression level(s) are indicative of the probability of recurrence of cancer via metastasis or survival outcome.

60. (Currently amended) The method of claim 32 wherein said ~~sample of breast cancer cells is ER+~~ assaying comprises determining the expression levels of HoxB13 and/or IL17BR mRNAs.

61. (Previously presented) The method of claim 6 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 or IL17BR sequences.

62. (Previously presented) The method of claim 14 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 or IL17BR sequences.

63. (Previously presented) The method of claim 23 wherein said assaying is by hybridization to a polynucleotide comprising sequences of at least 15 nucleotides from the 3' untranslated region, the coding region, or the 5' untranslated region, of human HoxB13 or IL17BR sequences.

64-66. (canceled) ~~The method of claim 6 wherein said assaying for expression comprises assaying for methylation of HoxB13 or IL17BR nucleic acid sequences.~~

65. (Previously presented) ~~—The method of claim 14 wherein said assaying for expression comprises assaying for methylation of HoxB13 or IL17BR nucleic acid sequences.~~

66. (Previously presented) ~~—The method of claim 23 wherein said assaying for expression comprises assaying for methylation of HoxB13 or IL17BR nucleic acid sequences.~~

67. (New) The method of claim 12 wherein said antiestrogen agent is tamoxifen.

68. (New) The method of claim 20 wherein said antiestrogen agent is tamoxifen.

69. (New) The method of claim 29 wherein said antiestrogen agent is tamoxifen.
70. (New) The method of claim 42 wherein said antiestrogen agent is tamoxifen.